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DOI:
10.1016/j.eururo.2014.02.031

Document Version
Peer reviewed version

Citation for published version (Harvard):
Bryan, RT, Kirby, R, O'Brien, T & Mostafid, H 2014, 'So much cost, such little progress', *European urology*, vol. 66, no. 2, pp. 263-264. https://doi.org/10.1016/j.eururo.2014.02.031

Editorial: SO MUCH COST, SUCH LITTLE PROGRESS

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Word count: 986

Keywords: Bladder cancer, economics, expense

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Urothelial bladder cancer (UBC) is burdensome for patients and expensive for healthcare providers [1]. Outcomes have changed little for three decades, despite significant improvements in 5-year survival rates for prostate and kidney cancers during this period [1]. Furthermore, patient pathways are complex, prolonged, and practiced in various permutations at every stage:

- The investigation of patients with suspected UBC requires multiple diagnostic procedures [2;3]; various combinations of tests are utilised [4].
- TURBT can performed by a number of different techniques with a number of different energy sources, and utilising a variety of optical image enhancement technologies [5].
- Further treatment may be required in the form of intravesical therapy with various agents, with or without chemohyperthermia or electromotive drug administration [3].
- Long-term surveillance is the mainstay of subsequent management [2;3]; various surveillance schedules are practiced [6].
- Surveillance may or may not utilize urinary biomarkers, and treatment of recurrence may be carried out in the office or the operating theatre [6].
- For curative intent, patients who present with or progress to MIBC are treated by radiotherapy [2;7], chemoradiotherapy [8], radical cystectomy (open, laparoscopic or robot-assisted), or neoadjuvant chemotherapy followed by radical cystectomy [2;7]; adjuvant chemotherapy is utilized in some units.

In this month's issue of European Urology, Svatek *et al* provide a review of the costs and other considerations for these approaches, and discuss key issues regarding the wider economics of

bladder cancer care [6]. This represents a useful overview for the practicing urologist. In particular, the authors demonstrate that there are large gaps in our knowledge regarding the efficacy and cost-effectiveness of these approaches and a lack of sufficiently-powered randomised controlled trials (RCTs), with expensive tools having crept into everyday practice without the necessary thorough evaluations. They highlight that there is a clear and urgent need for the development of new drugs for UBC, both NMIBC and MIBC. The prevalence of NMIBC and its protracted course compared to MIBC is such that the cumulative cost of care is thought to be even more substantial than MIBC [6], so the gains to be made in preventing recurrence and progression of NMIBC could be the most significant. Furthermore, the individual physician has the greatest impact on the cost of care of NMIBC, yet variation in treatment intensity does not impact survival or the avoidance of subsequent major interventions [6]. Other authors have recently highlighted these and other issues in bladder cancer care [1]. However, in order to make practice-changing recommendations, robust and detailed assessments of specific elements of these complicated pathways are required, utilizing complex modeling and statistics, and measures of cost-effectiveness. Such analyses have previously been undertaken in the UK in the form of Health Technology Assessments [4;9]. Reasonably, Svatek *et al* do not venture into this complex territory, but such health services research is urgently needed alongside basic and translational research and clinical trials [1]. Furthermore, the non-medical costs associated with UBC care (that are borne by patients, their families, their employers) and the costs associated with untimely deaths due to UBC are simply staggering [6]. Perhaps the treatment of UBC has far more impact on HRQoL than we have previously realised?

The Authors could have been more prescriptive in their conclusions to send a clearer message. For example, they present data that level 1 evidence and clinical guidelines are being ignored [1;6], yet fail to recommend that such evidence and guidelines be more closely adhered to. Perhaps we don't actually need more RCTs of BCG maintenance therapy, which are both expensive and protracted? Instead, would a better use of resources be to gain a clearer understanding of BCG's mechanism of action and the immunological milieu of the bladder tumour microenvironment, potentially leading to the development of new therapeutics for all UBC patients? NMIBC is also an ideal setting in which to assess the effectiveness of novel low toxicity therapeutics and/or chemopreventive agents administered long-term (and several such RCTs are in follow-up, eg. BOXIT, SELENIB), yet such strategies are not discussed by the Authors. As for urinary biomarkers, their real utility may not actually lie in their ability to detect new or recurrent disease, but in their ability to risk stratify patients early in their pathway so that they are investigated and managed more appropriately and expeditiously [10]. There is a lot that we could do now to redesign these pathways and interventions [10], yet there is a reluctance to change and a significant lack of research funding [1].

And it is this lack of research funding that underlies our complex and varied pathways. We don't actually have the robust evidence base to support a lot of what we do, and where the robust evidence and high grade recommendations exist, the uptake is poor (eg. single-shot intravesical mitomycin C [3], neoadjuvant platinum-based combination chemotherapy [7]) [6]. Consequently, a spectrum of alternatives is practiced by individual urologists and/or individual units, possibly accentuated in the USA by illogical reimbursement patterns [1]. The Authors' lack of decisive conclusions is therefore understandable.

If we are to tackle bladder cancer and improve outcomes, as we have done for prostate and kidney cancer, then we need to lobby for more funding for RCTs, translational science and health services research, and address the poor awareness of UBC among the general public and the nonurological scientific community [1]. And where are MIBC's innovative new drugs? It feels as though the pharmaceutical industry have deserted UBC in search of lower hanging fruit. These issues were specifically discussed amongst leading UK urologists and oncologists at The Royal Society of Medicine Section of Urology Annual Winter Meeting in January, and it was concluded that The Royal Society of Medicine, the British Association of Urological Surgeons, The Urology Foundation and Action on Bladder Cancer should endeavour to undertake a collaborative and concerted effort to advance the cause for bladder cancer patients. We need to make much more progress, perhaps improving cost-effectiveness along the way.

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